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10/645,913	08/21/2003	Michael M. Grunstein	RCHP-106US1	9590

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,913	GRUNSTEIN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *10, 23, and 27-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 11-22, and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response received January 8, 2007 is acknowledged.

Claims 1 and 14 have been amended.

Claims 44 and 45 have been added.

Claims 10, 23, and 27-43 stand withdrawn from consideration as being drawn to nonelected inventions. See 37 CFR 1.142(b) and MPEP § 821.03, for reasons of record set forth in the restriction requirement mailed April 17, 2006.

Newly submitted claims 44 and 45 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The newly submitted claims recite methods of administering nucleic acids to inhibit asthma. As such, the agent used in the method is structurally and mechanistically distinct from the elected invention of administering polypeptide agents that bind FcεRII and inhibit the binding of IgE to FcεRII, and as such the new claims comprise a patentably distinct method.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 44 and 45 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-9, 11-22 and 24-26 are under examination as they read on methods of inhibiting induction of an asthmatic state by administering an agent binds FcεRII and inhibits the binding of IgE to FcεRII.

2. The Declaration of inventors Michael Grunstein and Hakon Hakonarson received as part of the response of January 8, 2007 is acknowledged and will be discussed in conjunction with the rejections of record to which its subject matter is addressed.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2, 7-9, 11-15, 20-22, and 24-26 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The office action mailed October 4, 2006 states:

> The disclosure of the instant specification is not sufficient to enable a skilled artisan to practice the claimed invention without conducting an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).
>
> Regarding in vivo methods which rely on previously undescribed and generally unpredictable mechanisms, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)." The MPEP also states that physiological activity can be considered inherently unpredictable.
>
> Further, in Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), the court states "[W]here there is "no indication that one skilled in [the] art would accept without question statements [as to the effects of the claimed drug products] and no evidence has been presented to demonstrate that the claimed products do have those effects," an applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement" and "If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."
>
> With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

Applicant has recited methods of "preventing induction of the asthmatic state". The broadest reasonable interpretation of this phrase is that applicant's method is 100% effective in 100% of patients. The specification does not provide evidence that the claimed method is 100% effective. In fact, no working examples or in vivo data are disclosed, although in vitro data concerning cell lines and tissue sections are provided. A phase I (safety) clinical trial has been conducted wherein an anti-FcεRII (CD23) antibody was administered to human patients, but this study did not measure any of the signs and symptoms by which a determination could be made if the treatment had any clinical efficacy, such questions being deferred to phase II trials (Rosenwasser et al. J. Allergy Clin Immunol 2003, 112:563-570). Given that in vivo administration of anti-CD23 antibodies in nonhumans has been shown to decrease but not eliminate IgE (Flores-Romo et al., Science, 1993, 261:1038-1041), and since IgE is known to play a causative role in asthma (Hahn, US Patent 4,579,840, see particularly section V starting in column 12), it does not appear reasonable that applicant's claimed method can achieve 100% efficacy in all patients.

Further, the "prevention of an asthmatic state" is accomplished by administering an "agent" which inhibits binding of IgE to FcεRII. The specification teaches that it is preferable to perform the recited methods using an antibody that binds to FcεRII, but that that the invention also comprises administering any ligand of FcεRII including those ligands that are unknown. However, the breadth of the claims are even broader than administering any agent which is a ligand of FcεRII. Specifically, an agent that inhibits binding of IgE to FcεRII as is currently recited could be an anti-FcεRII antibody, or it could be an agent that does not bind FcεRII at all, since the binding specificity of the "agent" is not recited excepting dependent claims 6 and 19. For example, this broad genus of agents comprises antibodies which bind to IgE and prevent the binding of IgE to FcεRII, inhibitors of the expression of IgE and FcεRII such as antisense or RNAi molecules, and FcεRI, the high affinity receptor for IgE that is found on basophils and mast cells and competes for binding to IgE, and presumably encompasses unknown agents which inhibit the binding of IgE to FcεRII through unknown mechanisms.

Guidance or working examples concerning administering "agents" which inhibit the binding of IgE to FcεRII through undisclosed mechanisms do not appear to be present except for teachings concerning the administration of antibodies which bind FcεRII and thereby inhibit the binding of IgE to FcεRII. While the specification states that the invention encompasses ligands of FcεRII that are unknown, the specification cannot teach how to make such agents because by definition their composition or structure is not known. It logically follows if a substance is not known, the uses of that substance also cannot be known. Further, the claims are not limited to ligands that bind FcεRII. The specification does not appear to teach a generic mechanism concerning how "agents" inhibit the binding of IgE to FcεRII, nor does it appear to teach a screening mechanism that identifies the starting materials, process steps, and guidance as to the what molecules will be obtained upon completion of the screen for "agents" which inhibit IgE binding to FcεRII. As such, a skilled artisan would need to engage in unpredictable trial and error to generically identify "agents" that inhibit the binding of IgE to FcεRII for use in the instant methods.

Thus, in view of the quantity of experimentation necessary, the lack of sufficient guidance in the specification, the lack of working examples, the unpredictability of the art, and the breadth of the claims, a skilled artisan would be required to perform undue trials and errors to practice the claimed invention.

Applicant's arguments filed January 8, 2007 have been fully considered but they are not fully persuasive. Applicant first argues that no method of treatment is 100% effective, and while disagreeing with the office's interpretation of "prevention" has amended independent claim 1 to recite "inhibiting" rather than "preventing". Applicant then points to passages in the specification to support the amended claim language.

Applicant's claim amendment and arguments persuasively resolve the issue of "prevention", and therefore this ground of the rejection is withdrawn.

Applicant next argues that the scope of "agent" is intentionally broad and that a skilled artisan could identify such agents for use in the recited methods.

This argument is not persuasive for the reasons of record. Specifically, the specification does not appear to teach what such "agents" are other than antibodies that bind FcεRII (i.e. CD23). The specification specifically states that the disclosed invention encompasses agents both known and unknown (see particularly lines 16-19 of page 14). How can the specification disclose how to make and use something that is not known? Further, the starting materials for use in any method of screening for "agents" to be used in the methods of the instant invention are not disclosed, and therefore the skilled artisan has not been given sufficient guidance and direction concerning how to identify the unknown "agents" that are administered as part of the claimed method.

The rejection is maintained.

5. Claims 1, 2, 7-9, 11-15, 20-22, and 24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The office action mailed October 4, 2006 states:

> Applicant has claimed methods which recite the use of agents which inhibit the binding of IgE to an FcεRII receptor protein. This broad genus encompasses anti-FcεRII antibodies, and also encompasses *anything* that inhibits the interaction between IgE and FcεRII. Note that binding of the agent to FcεRII is not recited as the physical mechanism by which this inhibition is accomplished. As such, the claims read on agents such as antibodies which bind to IgE and prevent the binding of IgE to FcεRII, inhibitors of the expression of IgE and FcεRII such as antisense or RNAi molecules, and FcεRI, the high affinity receptor for IgE that is found on basophils and mast cells and competes for binding to IgE. To support this broad genus of agents, applicant has disclosed just a single agent, namely anti-FcεRII receptor protein antibodies.
>
> The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001, see especially page 1106 column 3).
>
> As discussed above, there are many structurally distinct "agents" which can inhibit the binding of IgE to FcεRII by unrelated mechanisms. The mechanistic pathways by which these agents inhibit binding are distinct functional properties of the agents even though all agents share the common result of inhibiting the interaction of IgE and FcεRII. Therefore, there does not appear to be a common structure or a common functional mechanistic pathway that is present in the genus of all agents that share the result of inhibiting the binding of IgE to FcεRII.

In The Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412) 19 F. 3d 1559, the court held that disclosure of a single member of a genus (rat insulin) did not provide adequate written support for the claimed genus (all mammalian insulins) and noted:

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene (in the instant case, an agent) does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes (agents) may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material."

The court has also noted that "Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

Therefore, it does not appear that the specification provides adequate written description for the genus of "agents" recited in the instant method claims, and as such applicant was not in possession of said genus at the time the application was filed.

Further, this application is a continuation of application 09/261,104, and the limitation "agents that inhibit IgE binding of IgE to an FcεRII receptor protein" is not an original claim limitation of the '104 application.

The specification teaches that:

> "The invention relates to a method of preventing induction of an asthmatic state in a human patient comprising administering to the human *an anti-Fc.epsilon.RII receptor protein ligand* suspended in a pharmaceutically acceptable carrier in an amount sufficient to inhibit binding of IgE to an anti-Fc.epsilon.RII receptor protein thereby preventing induction of the asthmatic state in the human. Preferably, the pharmaceutically acceptable carrier is physiological saline." (see lines 20-26 of page 13).

> "The invention should be construed to include any ligand that is currently either known or is heretofore unknown, which when bound to an Fc.epsilon.RII receptor protein on an airway smooth muscle cell of a mammal serves to alleviate an asthmatic state in the mammal.
>
> By the term "ligand" as used herein, is meant any natural or synthetic composition or compound which is capable of specifically binding to its cognate receptor protein, and when so bound, prevents binding of IgE to the cognate receptor protein, such that an asthmatic state is prevented or diminished. By way of example, an antibody which specifically binds to an Fc.epsilon.RII receptor protein on an airway smooth muscle cell and inhibits binding of IgE thereto, is termed an "anti-Fc.epsilon.RII receptor protein ligand." In this context, the Fc.epsilon.RII receptor protein is the "cognate receptor protein" for the ligand.
>
> By the term "anti-Fc.epsilon.RII receptor protein ligand" as used herein, is meant any natural or synthetic composition or compound which is capable of binding to an Fc.epsilon.RII receptor protein on an airway smooth muscle cell, which binding prevents binding of IgE to the cognate Fc.epsilon.RII receptor protein." (see lines 14-31 of page 14).

> "The *ligand* for use in the method of the invention may be any natural or synthetic composition or compound which *when bound to its cognate receptor* protein, *effects the inhibition of binding of IgE to the cognate receptor protein*. Thus, the ligand may be a protein, a peptide or a small molecule. The ligand may be administered to a cell as is, that is, as an isolated protein, an isolated peptide, a small molecule, or it may be administered to the cell in the form of an isolated nucleic acid sequence encoding the ligand." (see line 27 of page 15 to line 2 of page 16).

Based on the above, the specification does not teach "agents" but it does teach "ligands". Note that "ligands" are defined as binding to a cognate receptor, and the only cognate receptor that is discussed in the specification or is recited in the instant claims is FcεRII. As such, the disclosure as a whole teaches

that the compounds administered in applicant's disclosed methods of treating asthma bind to the cognate receptor protein FcεRII.

The instant claims recite administering an "agent" that "inhibits binding of IgE to a FcεRII receptor protein". The specification does not appear to define "agent" as being equivalent to "ligand". An "agent" can inhibit the binding of IgE to FcεRII even if it does not bind FcεRII. The specification does not appear to teach methods wherein any compound that does not act as a ligand for the cognate receptor FcεRII can be administered to treat patients. Thus the removal of FcεRII binding specificity from the claimed method appears to have broadened the claimed invention beyond what applicant disclosed the invention to be at the time the application was filed. This broadening does not appear to be supported by the specification as filed, and as such the instant claims comprise new matter.

Applicant's arguments filed January 8, 2007 have been fully considered but they are not persuasive. Applicant argues that the claim has been amended to recite that the "agent" binds to FcεRII and thus the "agent" can no longer be anything that inhibits the interaction of FcεRII and IgE.

The claim amendments to independent claims 1 and 14 to recite that the administered agent must bind (i.e. act as a ligand for) FcεRII have removed issues concerning the claiming of new matter. However, neither these amendments nor applicant's arguments address how the structure of the recited "agent" is correlated with the functional property of binding FcεRII and inhibiting IgE binding to FcεRII. As was discussed in the rejection of record, the specification explicitly contemplates the use of agents both known and unknown (lines 16-19 of page 14) in the instant methods. How can the instant inventors have possession of an "agent" that is unknown at the time the instant application was filed?

The rejection of record is maintained.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-9, 12-22, 25, and 26 stand rejected under 35 U.S.C. 102(e) as being anticipated by Reff et al. (US Patent 6,011,138).

The office action mailed October 4, 2006 states:

> Reff et al. teach methods of administering monoclonal anti-FcεRII (anti-CD23) antibodies that inhibit the binding of IgE to CD23 to humans for the treatment of asthma (see entire document, particularly the abstract, lines 57-60 of column 2, and lines 41-67 of column 38). These antibodies can be formulated into compositions comprising for administration via a variety of routes, with intravenous administration preferred (see lines 21-26 of column 40). Physiological saline solutions are taught for use with parenteral administration (see particularly from line 30 of column 43 to line 14 of column 44).
>
> Therefore, the prior art anticipates the claimed invention.

Applicant's arguments filed January 8, 2007 have been fully considered but they are not persuasive. Applicant argues that the copy of the declaration of inventors Michael Grunstein and Hakon Hakonarson submitted January 8, 2007 establishes that the instant inventors conceived and reduced to practice the claimed method prior to the disclosure of Reff et al.

This argument is not convincing, because the evidence cited in the declaration of inventors Michael Grunstein and Hakon Hakonarson as Exhibits A-F to support an earlier conception and reduction to practice have not been provided as part of applicant's response received January 8, 2007. Without these exhibits, no evidence to support the statements of inventors Michael Grunstein and Hakon Hakonarson that they conceived and reduced to practice the claimed invention prior to the disclosure of Reff et al. is present in the instant application. Therefore, this declaration has been found to be insufficient to antedate the disclosure of Reff et al. and the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 11, 14, and 24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Reff et al. (US Patent 6,011,138) in view of Cockcroft et al. (J. Allergy Clin. Immunol. 1987, 79:734-740).

The office action mailed October 4, 2006 states:

> The teachings of Reff et al. have been discussed supra. These teachings differ from the instant claimed invention in that administration of anti-CD23 antibodies is not taught in conjunction with other well known anti-asthmatic agents such as corticosteroids and sodium cromoglycate (cromolyn).
>
> Cockcroft et al. teach the administration of well known anti-asthmatic agents, and that administration of multiple anti-asthmatic agents offer an advantage because administration of only a single agent is often inadequate to clinically treat asthma symptoms (see entire document, particularly the abstract and discussion section). It is further taught that corticosteroids are desirable for combination therapy with anti-asthmatic agents since they have the advantageous property of being able to be administered prophylactically (see particularly the last sentence of the abstract and the last paragraph of the discussion on page 739).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to coadminister anti-CD23 antibodies as taught by Reff et al. and corticosteroids as taught by Cockcroft et al. because administration of any single agent may not be sufficient to control clinical asthma symptoms as taught by Cockcroft et al., with corticosteroids offering the particular advantage that they are an agent known to be effective in treating asthma that can be administered prophylactically.

Applicant's arguments filed January 8, 2007 have been fully considered but they are not persuasive. The argument is that the declaration of inventors Michael Grunstein and Hakon Hakonarson antedates the art of Reff et al., thus precluding a rejection.

This argument is not persuasive because as is explained above, evidence cited in the declaration as Exhibits A-F have not been provided as part of the response received January 8, 2007. Without this evidence to support the statements of inventors Michael Grunstein and Hakon Hakonarson, their declaration is not persuasive.

Therefore, the rejection is maintained.

10. Claims 1-9, 12-22, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flores-Romo et al. (Science, 1993, 261:1038-1041) in view of Mosley et al. (US Patent 5,599,905).

The office action mailed October 4, 2006 states:

Flores-Romo et al. taught that administering polyclonal antibodies that bind human CD23 (i.e. FcεRII) inhibits the synthesis of IgE both in vivo and in vitro, and that regulation of IgE synthesis by CD23 is important in allergic diseases (see entire document, particularly the abstract). This inhibition was observed for administered whole antibody as well as administered Fab fragments (see particularly Table 1). The antibodies were present in phosphate-buffered saline and were administered via a parenteral route, specifically intraperitoneal (see note 7 and the legend of Table 1). It is further taught that administration of anti-CD23 causes a reduction in the expression of CD23 on cells (see particularly figure 3 and the first full paragraph of the left column of page 1040). These teachings differ from the instant claimed invention in that Flores-Romo et al. do not teach that asthma is an allergic disease and in that the antibodies were not administered to a human patient.

Mosley et al teach that agents which suppress production of IgE are to be used in the treatment of human diseases such as allergic rhinitis, bronchial asthma, atopic dermatitis and gastrointestinal food allergy, and that intravenous administration is a preferred route for administering such agents to humans (see entire document, particularly lines 1-43 of column 16).

As such, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to administer the anti-CD23 antibodies of Flores-Romo et al. to humans to treat asthma. Motivation to do so at the time the invention was made comes from the teachings of Mosley et al. that agents which inhibit IgE production are preferentially administered intravenously for treating asthma and the teachings of Flores-Romo et al. that administering anti-CD23 antibodies inhibits IgE production in vivo.

Note that dependent claims 6 and 19 recite that anti-FcεRII receptor protein antibodies inhibit the binding of IgE to FcεRII. Further, any agent that decreases a patient's total IgE level and level of cellular FcεRII would necessarily inhibit the binding of IgE to FcεRII since the decreased expression levels make it less likely ligand-receptor pairs can be formed.

Applicant's arguments filed January 8, 2007 have been fully considered but they are not persuasive. Applicant argues against each reference in isolation, stating that neither reference teaches all recited claim limitations.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Given that the rejection has been set forth under 35 USC 103, it is true that neither reference, in isolation, teaches every recited claim limitation.

Applicant also argues that the agents disclosed by Flores-Romo et al. and Mosley et al. do not interfere with the actual binding of IgE to FcεRII, a limitation of the amended claims.

This argument is not persuasive because the anti-CD23 (i.e. anti-FcεRII) polyclonal antibodies of Flores-Romo et al. were demonstrated to bind the lectin domain of CD23 which is also the domain of CD23 that is responsible for binding IgE (see particularly Figure 2 and the middle column of page 1039).

The rejection of record is maintained.

11. Claims 11 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flores-Romo et al. (Science, 1993, 261:1038-1041) in view of Mosley et al. (US Patent 5,599,905) as applied to claims 1-7, 9, 12, 13, 14-20, 22, 25, and 26 above, and further in view of Cockcroft et al. (J. Allergy Clin. Immunol. 1987, 79:734-740).
The office action mailed October 4, 2006 states:

> The teachings of Flores-Romo et al. in view of Mosley et al. have been discussed supra. These teachings differ from the instant claimed invention in that administration of anti-CD23 antibodies is not taught in conjunction with other well known anti-asthmatic agents such as corticosteroids and sodium cromoglycate (cromolyn).
>
> Cockcroft et al. teach the administration of well known anti-asthmatic agents, and that administration of multiple anti-asthmatic agents offer an advantage because administration of only a single agent is often inadequate to clinically treat asthma symptoms (see entire document, particularly the abstract and discussion section). It is further taught that corticosteroids are desirable for combination therapy with anti-asthmatic agents since they have the advantageous property of being able to be administered prophylactically (see particularly the last sentence of the abstract and the last paragraph of the discussion on page 739).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to coadminister anti-CD23 antibodies as taught by Flores-Romo et al. and Mosley et al. and corticosteroids as taught by Cockcroft et al. because administration of any single agent may not be sufficient to control clinical asthma symptoms as taught by Cockcroft et al., with corticosteroids offering the particular advantage that they are an agent known to be effective in treating asthma that can be administered prophylactically.

Applicant's arguments filed January 8, 2007 have been fully considered but they are not persuasive. Applicant argues that the teachings of Cockcroft do not make up for the deficiencies of Flores-Romo et al. and Mosley et al. in teaching all recited limitations.

This argument is not persuasive for the reasons discussed supra, and therefore the rejection is maintained.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-9, 11-22, and 24-26 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,630,140. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are narrower in scope and thus anticipate the instant claims.

The office action mailed October 10, 2006 states:

> Specifically, the patented claims recite that administering an agent which inhibits the binding of IgE to FcεRII prevents induction of "a CD23 mediated asthmatic state" and that said administration is performed on "airway smooth muscle cells." The instant claims recite methods of preventing induction of an asthmatic state, a broader limitation since all asthmatic states are prevented rather than only ones that are mediated by CD23. Similarly, the agent administered in the instant claims can be administered anywhere rather than only being administered to airway smooth muscle cells as is recited in the patented claims. Thus the patented claims anticipate the instant invention because the patented claims recite a specific set of limitations encompassed by the generic language of the instant claims.

Applicant has acknowledged this rejection and to defer a decision on filing a terminal disclaimer until such time as all other pending rejections have been overcome.

The rejection is maintained.

14. No claims are allowable.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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April 3, 2007

4/7/07
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER